ALZHEIMER'S DISEASE
THE ALUMINIUM LINK

Alzheimer's disease is on the rise in many regions of the world due to environmental factors, but by increasing magnesium and calcium intake and reducing aluminium absorption the disease can be prevented and its symptoms reversed.

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Lear: *Does any here know me? This is not Lear.*
Does Lear walk thus, speak thus? Where are his eyes?
Either his notion weakens, his discernings
Are lethargied – Ha! Waking? 'Tis not so.
Who is it that can tell me who I am?

Fool: *Lear's shadow.*

William Shakespeare, *King Lear*

THE COSTS OF LONGEVITY

Life expectancies have risen dramatically over the past century. As a consequence, in both the developing and developed world, the number of elderly has undergone an unprecedented increase, with the proportion of the very old in the population doubling in one generation. Globally, in 1950 there were 214 million people aged 60 or over; by 2025 there probably will be one billion, a more than fourfold increase.[1] Although, of course, there are major advantages associated with this trend, there are also serious costs. Not only are more people surviving into old age and therefore increasing their chances of developing dementia, but those who do so are living longer after its onset.

Gruenberg[2] termed this paradox the "failure of success" because it was a major problem that was largely attributable to progress in medical care. As he and his colleagues pointed out, "the old man's friend, pneumonia, is dead—a victim of medical progress".[3] While this is an oversimplification, pneumonia is certainly less common than it used to be, as are many other diseases that were previously fatal to the elderly. As a consequence, 5–6 per cent of the USA population now has Alzheimer's disease or related dementia, some 4.5 million Americans. This figure is expected to rise to 14 million by 2050.[4]

Of course, dementia is not limited to the USA. For example, it has been estimated that, as of the year 2000, approximately eight million people in the European Union Member States had Alzheimer's disease. Since this disorder accounts for some 50 per cent of all dementia in people over sixty-five, total estimates for dementia in Europe are closer to 16 million. As in the USA, the population of Europe is ageing rapidly and the number of senile dementia cases increasing dramatically.[5] Clearly, in the Western world, dementia is not a rare problem. Indeed, Katzman and colleagues[6] have argued that, in those aged over seventy-five, new cases of dementia occur as frequently as myocardial infarction and twice as often as stroke.

Despite considerable hype from the pharmaceutical industry, there has been little real progress in either the prevention or the treatment of Alzheimer's disease. The estimated US$100 billion costs associated with the disease in the USA produce no cures and, if anything, by extending the life expectancy of the demented merely exacerbate the problem. The health bill for "warehousing" 4.5 million Alzheimer's patients in the USA is roughly equivalent to the cost of running 500 moderate-sized universities, providing higher education to some seven million students. The reader can decide which would be the better use for their taxes.

GENETIC PREDISPOSITION

Alzheimer's disease is named after Dr Alois Alzheimer, the first doctor to identify a patient (Auguste D.) suffering from this disorder, and then only after her death. What was

it about Auguste D.'s brain samples that Alzheimer found so striking and unusual? He noticed something in the slides that was extremely rare: gum-like clumps outside some cells and abnormal collections of proteins inside others; that is, plaques and tangles respectively. A fresh look at the recently rediscovered Auguste D. slides confirms Alzheimer's claims. Her cortex displayed what are now accepted as the classic pathological signs of the disease named after him: amyloid plaques and neurofibrillary tangles. Indeed, neurofibrillary tangles were described for the first time ever in this brain.[7]

It is now well known that such plaques and tangles are formed by the deposition of abnormal proteins, especially beta-amyloid and tau. The risk of developing Alzheimer's disease, therefore, rises and falls with the ability to prevent the formation and deposition of such proteins. This ability is, in part, genetic. The apolipoprotein (APO) E4 allele plays a key role in promoting Alzheimer's disease because of the inefficiency with which those possessing this genetic aberration can remove brain beta-amyloid and tau.[8]

Genetically, however, there is more to Alzheimer's disease than the APO E4 gene. To date, four genes have been identified as playing a role in either early- or late-onset Alzheimer's disease: beta-amyloid precursor protein, presenilin-1, presenilin-2, and apolipoprotein E genes.[9] Workers have linked most of these variants to familial early-onset Alzheimer's, but the APO E4 allele is a relatively common risk factor for developing late-onset Alzheimer's disease.[10] Considerable progress has been made in interpreting the significance of such genetic variants.

To illustrate, mutations in the presenilin-1 gene seem associated with increased super-oxide production and greater vulnerability to amyloid beta peptide toxicity.[11] Interestingly, mutations in the presenilin genes, which are linked to more than 40 per cent of all familial Alzheimer's cases, cause enhanced production of an abnormal form of beta-amyloid precursor protein.[12] This protein is longer than normal, aggregates more rapidly, kills neurons in culture more effectively and precipitates preferentially to form amyloid plaques. The same elongated protein also is produced as a result of mutations in the gene encoding beta-amyloid precursor protein.

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ENVIRONMENTAL VARIATIONS

There must be far more to Alzheimer's disease, however, than just genetics. There is no doubt the environment plays a key role in this illness. Multi-infarct dementia is common in Japan but Alzheimer's disease incidence seems to be much lower than in Europe.[13] This is unlikely to be due to racial variables because, in China, vascular dementia predominates in Beijing and Alzheimer's disease in Shanghai.[14]

At the regional scale, spatial variations in the incidence and prevalence of Alzheimer's disease are far greater. Two hospital-based studies[15] involving brain autopsies of every patient dying with dementia in Maracaibo, Venezuela, a city with a population of some 650,000, discovered only one Alzheimer's case in over a decade. In contrast, in the worst-affected Norwegian municipalities during the period 1974–1983, the median annual age-adjusted Alzheimer's disease mortality rates were between 44 and 55 per 100,000 for males and between 87 and 109 per 100,000 for females.[16] These figures suggest that Alzheimer's disease is at least 1,000 times more common in the municipalities along the south and southeastern coasts of Norway than in Maracaibo, Venezuela. Even within Norway itself, Alzheimer's mortality was higher by a factor of 15 in some municipalities than in others during this period.

Studies of temporal change in dementia incidence are expensive and complex and involve extensive fieldwork. As a result, they are rare. The best study probably comes from Lundy, Sweden,[17] where the entire population was medically examined several times between 1947 and 1972. Interestingly, all levels of dementia were found to have decreased by the end of the period. This seems unusual, since more recent studies conducted in the United States,[18] England,[19] Australia,[20] Canada[21] and Norway[22] all suggest that Alzheimer's disease is becoming increasingly common.

Two recent research projects have demonstrated that migration greatly influences the prevalence rates of dementia. Graves and co-workers[23] established that, in the Japanese Americans of King County, Washington State, dementia was more common than in Japan. In addition, the distribution of subtypes of dementia in Japanese Americans was found to be much more like that of North American and European Caucasians than of Japanese residing in their homeland. As a result, Alzheimer's disease was more common and vascular dementia less prevalent in Japanese Americans than might have been expected. A similar study conducted in Indianapolis and Ibadan, Nigeria, by Hendrie and co-workers[24] established that Alzheimer's disease was more than twice as common in African Americans than in Nigerian Yoruba of the same gender and age ranges.

In summary, globally and regionally Alzheimer's disease does not have a random, relatively uniform spatial pattern. It appears to be increasing faster than the population is ageing and its incidence and prevalence are greatly affected by migration. In short, it shows none of the expected geographical characteristics of a primarily genetic disease.

KEY RISK FACTORS

In their book *Genome*, Bishop and Waldholz[25] argue that: "...aberrant genes do not, in and of themselves, cause disease. By and large their impact on an individual's health is minimal until the person is plunged into a harmful environment." The significance of an aberrant gene therefore depends upon location and lifestyle; that is, on geography.

The preceding review of the literature establishes that the "harmful environments" that increase the significance of inheritance of the APO E4 gene and other Alzheimer's-related genetic aberrations have two very important characteristics. They

display very clear spatial variations, and appear to be increasing quite rapidly in number. There is extensive evidence to suggest that such environments are areas where drinking water is high in dissolved aluminium [aluminum] (especially in its monomeric form) together with depressed levels of magnesium and calcium. This water is also typically low in silicic acid. These conditions occur where low-alkalinity surface waters have very little ability to buffer the impacts of acid rain, one of which is increased aluminium solubility.[26] In such low-alkalinity, high-acid-rain regions, rising levels of dissolved aluminium, found in both soil water and run-off, are resulting in widespread ecological damage. It appears that this element is also the dominant environmental risk factor in Alzheimer's disease.

Clear evidence was provided in 1988 that excess aluminium in potable water can affect memory. An accident at a water supply plant at Camelford in Cornwall, England, resulted in water that contained enormously elevated levels of aluminium sulphate being drunk by the local population. Memory loss was an extremely common complaint amongst those unfortunate enough to use such contaminated water.[27]

Significant evidence of the link between dementia and aluminium also comes from McLachlan's Ontario study involving 668 autopsy-verified Alzheimer's brains.[28] These demonstrated that the risk of developing Alzheimer's disease had been about 2.5 times greater in individuals from communities that drank water that contained more than 100 mcg per litre of aluminium than it had been in those from areas where the potable water had contained less than this level of aluminium. McLachlan's results were even more spectacular for those who had drunk water that contained 175 mcg per litre of aluminium. Depending on how those patients were grouped, the odds ratio of developing Alzheimer's disease varied from 6.7 to 8.14; that is, their brains were some 7–8 times more likely to show the characteristic signs of Alzheimer's disease if such patients had normally consumed water that was very high in aluminium.

Several authors have attempted to quantify the strength of the association between Alzheimer's disease and aluminium. Forbes and McLachlan,[29] for example, studied this link in the very elderly, those aged eighty-five years or more. They discovered that, after controlling for six other factors such as fluoride, silicic acid, iron, pH and turbidity, those living in districts that supplied drinking water that contained more than 250 mcg of aluminium per litre were almost 10 times more likely to develop Alzheimer's disease. This confirmed an earlier Ontario longitudinal study[30] which established that men aged seventy-five years and older, who were drinking water containing at least 0.0847 mg per litre of aluminium, were 1.72 times as likely to show impaired mental functioning. Similarly, after statistical control for five other variables, Alzheimer's mortality displayed an odds ratio of 3.54 for those who had drunk water that contained at least 0.336 mg per litre of aluminium.[31]

A more recent eight-year longitudinal study involved 3,777 people aged sixty-five years and older who lived in southwest France in 1988–1989. It confirmed that double the risk of developing Alzheimer's disease occurred in those who drank water with an aluminium concentration greater than 0.1 mg per litre.[32]

Looking for a link between Alzheimer's disease and total drinking water aluminium may be too simplistic. In 2000, Gauthier and co-workers[33] described a case control study in which the chemical characteristics of the water historically drunk by 58 elderly Alzheimer's patients were compared with those of potable water used by age- and gender-matched non-demented controls. This was conducted in the Saguenay-Lac-Saint-Jean region of Quebec. Aluminium (Al) specification was assessed using standard analytical protocols. Long-term drinking water exposure (from 1945 to the onset of Alzheimer's disease) was estimated for total aluminium, total dissolved aluminium, monomeric organic and inorganic aluminium, polymeric aluminium and five other species of this metal. While there was no obvious relationship between total aluminium in potable water and Alzheimer's disease, after adjustment for educational level, family cases of the disorder and the APO E4 allele, exposure to monomeric aluminium clearly was associated with this form of dementia (odds ratio 2.67).

The negative impact of aluminium, however, appears to be mitigated by silicic acid, calcium and magnesium.

The importance of monomeric (single molecule) aluminium has been confirmed again by a more recent study conducted by Prolo and colleagues[34] in northwest Italy, where the drinking water contained between 5 mcg and 1,220 mcg per litre of total aluminium. Levels of monomeric aluminium (the type of this element most easily able to enter human cells) ranged from 5 mcg to 300 mcg per litre. These researchers from the University of California at Los Angeles established that Alzheimer's disease was most common where drinking water levels of monomeric aluminium were highest. They also discovered that monomeric aluminium interfered with cell function in cultures, accelerating cell death especially in the presence of beta-amyloid protein.

The great bulk of evidence from numerous geographical and epidemiological studies, therefore, supports a strong link between aluminium consumption, especially monomeric aluminium from drinking water, and an elevated incidence of Alzheimer's disease. The negative impact of aluminium, however, appears to be mitigated by silicic acid, calcium and magnesium, especially in potable water with a pH of between 7.85 and 8.05. Acidic drinking water that is high in aluminium and lacking in silicic acid, calcium and magnesium seems to be particularly dangerous. Fluoride is a well-established antagonist of aluminium and may also protect against Alzheimer's disease when the water pH is high; but unfortunately, elevated water fluoride levels are known to cause other health problems.

HOW ALUMINIUM CAUSES ALZHEIMER'S DISEASE

If aluminium causes Alzheimer's disease, how does it trigger this form of dementia? It seems that individuals who inherit the APO E4 gene(s) are less capable than the general population of removing the beta-amyloid and tau brain proteins that form the bulk of neuritic plaques and neurofibrillary tangles. As a result, such people are at higher risk of developing Alzheimer's disease in regions that promote the deposition of beta-amyloid and tau. Such "harmful environments" are those in which the potable water is acidic, high in monomeric aluminium and lacks silicic acid, calcium and magnesium. Under such circumstances, aluminium can enter the brain and impair the enzyme choline acetyltransferase,

creating an acetylcholine deficiency. A shortage of acetylcholine encourages the growth of senile plaques. Similarly, aluminium interferes with the enzymes calcium/calmodulin kinase II and alkaline phosphatase, promoting the formation of neurofibrillary tangles. Plaques and tangles created in this manner are the hallmarks of Alzheimer's disease. Such relationships, therefore, explain why this form of dementia is most common in regions of high water acidity, in those members of the population that carry the APO E4 isoform.

There is, however, more to Alzheimer's disease than plaques and tangles. David Shenk,[35] in his interesting book *The Forgetting*, describes Alzheimer's disease as "death by a thousand subtractions". The scientific evidence appears to support this characterisation. In 1980, for example, Barry Reisberg,[36,37] a neurologist from New York University, established the presence of an inverse relationship between the progressive stages of Alzheimer's disease and those of infant and childhood development. He demonstrated that as the symptoms of this form of senile dementia worsen, the patient begins to lose abilities in cognition, coordination, behaviour, language and feeding, in the reverse order in which they were acquired in the early years of life. In the final stage of the disorder, the patient becomes infant-like and can no longer walk, sit up without assistance, smile or hold up their head. Reisberg called this process of a thousand subtractions "retrogenesis", meaning "back to birth".

Although retrogenesis is not a perfect reversal, neurological tests do show that, as Alzheimer's disease progresses, there is an almost precise inverse relationship in neurologic reflexes, brain glucose metabolism and EEG activity. As the disorder worsens, all these abilities decline. Such evidence led Reisberg to present a picture of the brain as a giant ball of string wound up in infancy and childhood but unwound by Alzheimer's disease. From birth and throughout childhood and beyond, the ball grows rapidly, but in Alzheimer's it is unravelled in reverse, slowly but surely reducing the ability of the brain to function.

In Alzheimer's disease, brain damage appears to begin in the most recently and least myelinated area of the brain, specifically in the hippocampus. As a consequence, the first symptoms of developing Alzheimer's are losses of recent memories. From the hippocampus, demyelinisation begins to impact on the frontal cortex, adversely affecting concentration, abstract thought and planning ability. This reverse myelinisation relentlessly continues, unwinding the "ball of string" in a very predictable manner until the primary motor area is finally affected and the late-stage Alzheimer's patient is again infantile, unable to speak, sit up unassisted or hold up their own head.

Interestingly, aluminium is known to damage myelin in numerous ways. Animal experiments clearly demonstrate that aluminium can alter the nature of myelin, accelerate its oxidation rates and promote its rapid loss from the hippocampus and spinal cord. Exactly how these procedures occur is uncertain. In a study of brains from monkeys chronically administered aluminium, Sarin and colleagues[38] were able to show, however, that this metal had inhibited three membrane-bound enzymes: specifically Na+K+ ATPase, acetylcholinesterase and, most interestingly, the myelin-specific enzyme 2',3'-cyclic nucleotide phosphohydrolase. This inhibition causes a rapid thinning of the myelin sheath in both rats[39] and mice,[40] and it can alter its composition by increasing galactolipids and so make myelin more prone to oxidation.[41,42] It does not seem much of a step to suggest that these destructive processes probably lie behind the demyelinisation and associated retrogenesis seen in Alzheimer's patients.

Beyond this, aluminium also inhibits the enzyme phospholipase A2, probably causing brain membrane dysfunctions, and seems to cause depression of antioxidant status by reducing levels of brain glutathione peroxidase, superoxide dismutase and catalase. As a result, the lipid peroxidation of cell membranes by free radicals is accelerated.[43]

The biochemical evidence therefore is very good in that in individuals who have a depressed calcium and magnesium intake combined with abnormally high aluminium absorption, some enzymatic processes are inhibited. This inhibition is most likely to occur in enzymes that have aluminium antagonists, such as calcium, magnesium and iron, as co-factors. It is not surprising, then, that since the end result of such enzyme inhibition is Alzheimer's disease, patients with this form of dementia experience a wide variety of biochemical abnormalities, 11 of which are discussed in some detail in the author's book, *What Really Causes Alzheimer's Disease*.[44] This is why no drug will ever prevent or reverse this form of dementia, unless it prevents aluminium absorption by the body.[45]

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AVOIDING ALZHEIMER'S DISEASE

Reducing Social Risk

Exposure to acidic water that contains elevated aluminium and depressed calcium, magnesium and silicic acid levels appears to promote Alzheimer's disease.

One might naively expect that it would be a relatively simple matter to pass legislation reducing levels of aluminium in, and promoting the addition of calcium, magnesium and perhaps silicic acid to, drinking water. Not only do governments show little interest in increasing the magnesium content of drinking water, they routinely allow the use of aluminium sulphate as a flocculant by water treatment plants. This practice reduces the amount of sediment in the water supply but greatly increases levels of dissolved aluminium, especially if the water is acidic.[46] Clearly, aluminium sulphate must be replaced by alternatives.

The Western diet promotes Alzheimer's disease in three distinct ways. First, it tends to be deficient in calcium and magnesium,[47] making those who eat it very susceptible to aluminium toxicity. Second, many foods are canned, wrapped and/or cooked in aluminium. The more acidic the food, the more easily it appears to dissolve this metal. Third, maltol is added to many processed foods in an attempt to "improve" flavour.[48] Maltol greatly increases aluminium's ability to cross the blood-brain barrier and

interfere with brain enzymes. Indeed, when researchers want to study a rabbit whose brain has been badly damaged by Alzheimer's-like plaques and tangles, they feed maltol to it.[49] There is no logical reason why maltol should be allowed to be routinely added to hot chocolate, beer, some commercially baked goods and many other products.

Reducing Personal Risk

For most of those reading this article, the average day will begin with a shower. If the water used is acidic and deficient in calcium and magnesium, it is possible that it will be a source of aluminium that enters the body through the pores and nose. This exposure to aluminium is most likely if the water supplier uses aluminium sulphate as a flocculant to remove sediment. Once dried off, most readers will smear their bodies with a layer of aluminium provided by antiperspirants and deodorants.[50] How much of this aluminium passes through the skin into the body is unclear, but McGrath[51] has argued that underarm shaving and frequent use of antiperspirants and deodorants seem linked to an early age of breast cancer diagnosis.

British researchers[52, 53] provided evidence to support the feasibility of McGrath's hypothesis, reporting traces of parabens in every tissue sample taken from 20 different breast tumours. Parabens are chemicals used in deodorants and other cosmetics that can mimic oestrogen. The hormone oestrogen is known to encourage breast tumour growth. Clearly, parabens can enter the body from deodorants and it is possible that aluminium can do the same. Deodorants with a herbal base do not usually contain these toxins.

Then comes breakfast. Tea, coffee and hot chocolate are usually made with water from the tap. It is important not to use soft, acidic water which is likely to contain monomeric aluminium. Most water supply companies will provide chemical analyses, allowing the assessment of the aluminium, calcium and magnesium content of their product. If not, private companies can conduct such analyses relatively cheaply. If colas or fruit juices are drunk, they are likely to have come from cans. These are typically made of aluminium. The longer the drink has been in the can, the higher the aluminium levels in it are likely to be.[54] In addition to any aluminium it contains, hot chocolate is likely to be "enhanced" with maltol, so increasing the likelihood that this metal will reach the brain. Similarly, tea brewed in acidic water or flavoured with lemon juice contains significantly higher levels of bioavailable aluminium than normal, because the metal contained in the leaves is more soluble in water with a low pH.[55]

After breakfast comes lunch, dinner and a variety of snacks. Junk food, because it is so heavily processed, is usually a very poor source of minerals, including calcium and magnesium. The average British and North American diet contains less than half the calcium and magnesium required to avoid the associated deficiency illnesses, including Alzheimer's disease.

The best way to address this problem is to eat many of the mineral-enriched foods such as salmon, sardines, broccoli, spinach and bok choy, for example, which are all high in calcium.[56, 57] Pumpkin seeds, almonds, Brazil nuts and wholegrain brown rice are good sources of magnesium.[58] Certain supplements, especially mineral ascorbates, provide high levels of both calcium and magnesium. Alacer Corporation of Foothill Ranch, California, a company with which I have no financial associations, provides excellent mineral ascorbate products. One tablet of Super-Gram II, for example, contains four per cent of the calcium and eight per cent of the magnesium recommended daily allowance. Emer'Gen-C is a fizzing drink mix that is pleasant to take when added to water. It provides 1,000 mg of vitamin C and 32 mineral complexes, including calcium and magnesium. Alacer's products were used in the Joint Russian Committee on World Health research projects that produced a marked reversal of memory loss in the elderly.[59, 60, 61] ∞

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About the Author:

Harold D. Foster, PhD, was born and educated in England. He specialised in geology and geography, earning a BSc in 1964 from University College London and a PhD in 1968 from London University. A Canadian by choice, he has been a faculty member in the Department of Geography, University of Victoria, British Columbia, Canada, since 1967.

A tenured professor, Dr Foster has authored or edited some 245 publications, the majority of which focus on reducing disaster losses or identifying the causes of chronic disease or longevity. He has published hypotheses on the origins of numerous diseases including myocardial infarction, SIDS, cancer, diabetes, schizophrenia, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Alzheimer's and Parkinson's diseases, stroke and AIDS.

His numerous books include: *Disaster Planning: The Preservation of Life and Property* (Springer Verlag, New York, 1980); *Reducing Cancer Mortality: A Geographical Perspective* (Western Geographical Press, Victoria, 1986); *The Ozymandias Principles: Thirty-one Strategies for Surviving Change* (Southdowne Press, Victoria, Canada, 1997); *What Really Causes AIDS* (Trafford Publishing, Victoria, 2002; reviewed in *NEXUS* 10/05), *What Really Causes Schizophrenia* (Trafford, 2003; reviewed in 11/02); and *What Really Causes Alzheimer's Disease* (Trafford, 2004; reviewed in 12/03).

Dr Foster is Associate Editor of the *Journal of Orthomolecular Medicine*, and was named Orthomolecular Doctor of the Year (2004–2005) by The International Society for Orthomolecular Medicine. He is a member of the board of the International Schizophrenia Foundation and is also a member of the Science Advisory Panel for the Healthy Water Association.

Every day, Dr Foster makes a point of taking at least the recommended daily allowance of the known essential nutrients. He is also currently pursuing offers for his suggested nutrient mixture to be produced for use in clinical trials with AIDS patients.

For a more detailed résumé, visit Dr Foster's website, http://www.hdfoster.com. Copies of several of his books can be freely downloaded from his website.

Editor's Note:

Due to space constraints we are not able to reprint Dr Foster's endnotes accompanying this article; however, these can be accessed via his website, http://www.hdfoster.com.